A Study of Fractional Test Meals in Cases of Dyspepsia.

by

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Being a study of the fractional test meal findings in 284 cases of dyspepsia, including 100 cases of duodenal ulcer, submitted as a thesis for the M.D. Edinburgh.

The aims of the investigation described below were as follows:-

I. To investigate the fractional test meal findings in patients admitted to hospital with dyspepsia and given a standard test meal using a carefully standardised technique throughout.

2. To investigate the relationship, if any, between the clinical picture, under hospital observation, of the dyspeptic patient, and the test meal findings, and to compare and contrast the results with those of other workers in similar states, more particularly with regard to peptic ulceration. Arising from this a study of the various theories of gastric secretion and neutralisation was made.

3. To ascertain the value of the fractional test meal as an aid to diagnosis.

Between Feb. 1943 and Feb. 1946, the Author was serving, firstly, in a R.N. Auxillary Hospital in Scotland and secondly in a similar type of, but smaller institution in Belgium. The cases described were investigated during this time by the Author and all clinical data was obtained and all the laboratory investigations made by the Author in person, using a carefully standardised technique. It is certain, therefore, that in these cases the investigations have been carried out with uniformity of method, and that it is possible

to compare one with another without the fear that small alterations in technique may have led to different findings. The writer has found that in some hospitals nowadays the investigation of cases of dyspepsia leaves much to be desired. Radiography is accepted as the diagnostic criterion but a test meal is often performed in the Out Patient department under far from ideal or standardised conditions and the patient given some such label as hyperchlorhydria, no other information being apparently obtained from the test. Cases have also been known in which a patient has consumed hydrochloric acid and pepsin for years without benefit after being diagnosed as a case of achlorhydria following one oatmeal gruel meal.

From the very early days of the recent War it was evident that dyspepsia- particularly dyspepsia due to duodenal ulceration,-was going to prove a major medical problem in the Royal Navy. Cases of dyspepsia far outnumbered any of the other serious medical complaints. Wade(I) in one R.N. Auxillary hospital alone describes I003 cases of dyspepsia as having been admitted between Oct. I939 and Sept. I94I this constituting 9% of all admissions. No fewer than 45% of these cases proved to be peptic ulceration confirmed by radiological findings, whilst the figure rose to 56% of cases of previously proved ulcers, histories of perforation etc. not at present giving positive radiological findings were included.

The same author quotes published findings from other Service hospitals in which the proportion of proved ulcers to cases of dyspepsia admitted was about the same. In Wade's series of cases 25% were aged between 2I - 25 years.

Although all three Services had to deal with enormous numbers of cases of dyspepsia during the War, the problem was perhaps most acute in the Navy. Large numbers of smaller ships had perforce to spend long periods at sea without a medical officer being either on board or available, nor was it usually possible to make any divergence from duty to land a sick man. Apart from humanitarian reasons, the effect on morale of a man dying from a perforated ulcer away from all medical help was likely to be unfortunate in a ship's company. It was probably as much for this reason as for any other that the Admiralty decided in March I94I, that all proved cases of peptic ulceration together with cases with a previous history of proved ulceration without present positive radiological findings, but with recurrence of symptoms, should be invalided from the Service. Exceptions were made only in the case of highly trained men who could be usefully employed ashore.

It will be seen from the above that the problem facing Service medical officers was a large one and that, for those who spent some time in a Naval hospital, there were excellent opportunities for

studying the various aspects of ulceration, particularly that due to peptic ulceration.

Although exact figures are not available, a large number (probably a vast majority) of cases of dyspepsia came from smaller ships. During 27 months spent in a large cruiser, employed on arduous duties, the writer found cases of dyspepsia, other than those with trivial and transient symptoms, were comparatively rare amongst a ship's company of over 900. During this period only 5 men had to be sent to hospital with dyspepsia--a very low figure when it is remembered that, with replacements and drafts, about 1300 men served for various periods in the ship during this time.

Classification.

For the purpose of this investigation the cases were divided into the following:-
1. Duodenal Ulcers. 2. Gastric Ulcers. 3. Anastamotic Ulcers. 4. Gastritis. 5. Gastro-Duodenitis. 6. Duodenitis. 7. Functional Dyspepsia. 8. Nervous dyspepsia. 9. Miscellaneous. The last group which was not large enough to divide into its component parts, consisted of a number of cases of reflex dyspepsia from such causes as chronic appendicitis, adhesions, gall stones, and other causes including one carcinama of the stomach.

The above divisions will be further discussed but it may be mentioned here that there were 100 cases of duodenal ulcer and

that groups 7 and 8 comprised III cases.
It is perhaps worthy of note that although there are a number of published results of fractional analysis in a series of cases all with the same diagnosis, ie IOO cases of duodenal ulcer or IOO cases of gastric ulcer, or the results obtained from a number of healthy men, the author has been unable to find in the literature any record of fractional analysis results where the patients had in common only the fact that they suffered from more or less severe dyspepsia. The comparison of the fractional analysis charts of these patients is interesting in view of the ultimate diagnosis, and is perhaps valuable in that it is certain that a uniform technique was followed throughout.

Although in some of these cases the diagnosis arrived at was a probable diagnosis rather than a certain diagnosis, the fact that the fractional analysis findings of these patients can be compared with those from cases of proved organic disease is useful in demonstrating to what extent fractional analysis can be used as an aid to diagnosis. The diagnosis of all cases of dyspepsia in which it is not possible to demonstrate organic disease beyond doubt must of course remain a matter of opinion based on the lack of positive findings.

Diagnostic Methods Used.

In view of the ultimate disposal of these cases and the necessity of balancing the shortage of man power with the need to preserve an efficient fighting Service, accurate diagnosis was essential and yet War time conditions had to be taken into account in evolving a diagnostic technique. Nursing staff, although adequate in numbers, was largely inexperienced and the various emergencies of warfare had to be taken into account as being liable on occasions to play havoc with routine. A case was, however, considered to be adequately diagnosed if the following procedure was carried out :-

I. A careful history of the case, including history of other illnesses and family history, was taken.

2. A thorough physical examination was made.

3. Laboratory investigations were made which included an examination of the urine, a full blood count and examination of the stained film in all but the most trivial cases, a fractional test meal (oatmeal gruel), details of which will be described later, with a histamine gastric analysis later in cases of achlorhydria. In addition to the above various other biochemical examinations were made as were appropriate to the individual cases, including Kahn or Wassermann reactions, examination of stools for pathogenic bacteria, tests of renal function etc.

Examination of the stools for occult blood was made in a number of the cases; too much reliance was not however placed on positive findings, as it was found that there were too many sources of error which were liable to creep in and make the test unreliable as an aid to diagnosis. Amongst the various fallacies may be mentioned errors of diet due to inexperience of nurses and non co-operation of the patients, bleeding gums often due to mild Vincents infection, which is a very common complaint of the sailor, and other incidental sources of haemorrhage including on one occasion an unrevealed epistaxis.

4. Radiological Examination included the screening of every case and palpation of the stomach and duodenum after a barium meal as well as the taking of a series of films.

With regard to the radiological findings it is considered that in diagnosing the presence of an ulcer, the demonstration of an ulcer crater is not absolutely essential providing that :-

(a) The clinical picture is present

(b) There is indirect evidence of ulcer.

5. Cases diagnosed as Nervous Dyspepsia were usually referred to the Psychiatrist for opinion.

Reasons for adopting the Oatmeal gruel meal (Boas or Rehfuss meal) as a standard for fractional gastric analysis.

The three principal types of test meal are the Ewald meal of tea and toast,often employed in the single hour method (now obsolete),the oatmeal gruel meal of Boas or Rehfuss, using a small bore tube and repeated aspirations of stomach contents, and the alcohol meal,also with repeated aspirations but using a 7% solution of alcohol in place of the gruel.

The chief objections of the Ewald meal are blocking of the tube by small pieces of toast,the brown dextrin colour of the specimens,and the variations in the methods used by the different authorities which have made the setting of a standard of normality impossible.

Strong alcohol inhibits the secretion of gastric juice but produces a copious secretion of thin mucous; weak alcohol,however,stimulates the secretion of gastric juice and produces juice of high acidity and low peptic power. A 7% solution of alcohol is used extensively as a test meal on the Continent. The author was priveleged to be present at an interrogation of the Surgeon Admiral in charge of the German Naval Medical Service and was informed that the Germans used the alcohol meal exclusively,other methods being considered out of date.

Although specimens obtained by this method are easy to titrate as the fluid is clear, the method has some drawbacks. There is a wide variation in the practice of this test and satisfactory normal standards are lacking. Also the procedure recommended by Bloomfield and Keefer (2) of the aspiration of a specimen every IO minutes, gives results in which the variations in the emptying rate are very varied and of little significance. Hence one of the more valuable items of information derived from fractional gastric analysis is lost.

The oatmeal gruel meal, used extensively by Rehfuss of Chicago, and called by some writers the Boas meal, gives a plentiful secretion of gastric juice of moderately high acidity and high peptic power. The meal is easy to standardise and to administer and the specimens are not difficult to titrate. Moreover the observations of Bennett and Ryle (3) on IOO healthy male students at Guy's Hospital have given a standard in so far as the average fractional gastric analysis in healthy young males has been worked out and recorded. These figures are usually represented in a gastric analysis chart as a shaded portion.

Eusterman and Balfour (4) have recorded an elaboration of this, showing a standard of normal for males and females at various ages.

The only serious objection to the oatmeal gruel meal, seems to be, that a certain number of cases are meal refractory and an apparent achlorhydria is found. In the author's series of cases, all patients with achlorhydria were given, after a few days, a further test in which the subcutaneous injection of histamine was employed as a stimulant to gastric secretion. Details of this will be given later.

Technique used for fractional gastric analysis.

A uniform technique was employed throughout. All drugs were prohibited for two days prior to the test. The patient was confined to bed and at 5 P.M on the day before the test was given a light meal. At 9 P.M. two charcoal biscuits were given. Early the next morning screens were placed round the bed and the patient was protected as far as possible from the sight and smell of food. At 8 A.M. a Ryles tube was passed. It is not necessary to describe here the details of this, but it may be mentioned that the best results were obtained by explaining to the patient what was necessary and then giving him the tube and letting him perform the operation himself. No lubricant was used and in few cases was any difficulty found. The bulbous end of the tube must rest in the lower part of the stomach.

The whole of the fasting stomach contents was then removed by aspiration, the patient being turned from side to side and put into various positions to ensure that this was so. The stomach having been emptied, the patient was given the meal to drink. The meal consisted of oatmeal gruel made by adding two tablespoonfuls of fine oatmeal added to a ~~pint~~ quart of water and then boiling it gently down until the total volume was one pint. The meal was then strained through fine muslin.

An alteration on the technique used by Rehfuss and others was now made in that instead of the subsequent specimens being taken every I5 minutes, they were taken every 30 minutes for 3 hours. After experimenting with various types of test meal it was considered that the taking of specimens every I5 minutes was liable to cause too much interference with and disturbance of the patient, doubled the work both in the ward and the laboratory, and frequently showed small variations in the curve of acidity which spoilt the broad picture of what was happening. By taking half hourly specimens the patient was able to relax quietly behind the screens, read a book, and forget about the presence of the tube, and it was felt that this method gave adequate information and was preferable in

many ways to the I5 minute technique usually employed.

About I0 -I5 cc of stomach contents were removed at each aspiration and placed in numbered tubes. After aspiration a small quantity of air was blown down the tube and the aspirating syringe was washed out with distilled water.

During the time that the tube was in position the patient was given a sputum mug and told that he must not swallow his saliva but must expectorate it into the mug. This avoided to a large extent the neutralising effect of saliva.

At the end of three hours the tube was withdrawn and the six specimens together with the resting juice removed to the laboratory.

The resting juice was measured, and it, and the other specimens, were examined as a routine for general appearance odour, traces of charcoal, mucus, bile, blood, pus, debris and any other abnormal constituent including lactic acid if the circumstances warranted it.

Then 5cc of the resting juice and of each of the other specimens were transferred to separate beakers by a pipette, the latter being washed out each time with distilled water and the washings added to the appropriate beakers.

Excess of mucus sometimes caused difficulty in measuring, but as will be seen in the recorded results this was not often present.

Two drops of each of the folowing indicators was then added to each of the beakers:-

I. Topfers Reagent.(di-methyl-amino-azo-benzene) an indicator with a pH range of 2.9 to 4.2.

2. Phenolphthalein--I% alcoholic solution with a pH range of 8.3 to I0.0.

Each specimen was then titrated against N/I0 NaOH. The Topfers reagent in the presence of free HCl gives a bright pink colour and the NaOH was added until a persistent bright canary colour was obtained,the burette reading then being taken. The canary yellow colour appears when all the free HCl is neutralised. The titration was then continued until a persistent bright pink colour appears from the phenolphthalein indicator and a second reading was made. The difference between the two readings gave the amount of weak and combined acids and the two figures added together gave the total acidity.

Finally the specimens were tested for the presence of the meal as represented by starch,by adding a drop of iodine solution and seing if a blue colour resulted.

The term "combined"acids used above includes acid combined with proteins,with enzymes and with mineral bases in the form of acid salts and also free organic acids.

The results were shown in the form of a graph, the free acid and total acid figures being expressed in terms of the number of cubic centimetres of decinormal sodium hyroxide solution required to neutralise I00 cc of the ~~test~~ gastric contents specimen being titrated. This figure was plotted against the time of aspirating the specimen in half hours with the resting juice being shown as zero hours.

The above method using Topfers reagent and phenolphthalein was found to be quite satisfactory and trials with other indicators such as thymol blue did not show the latter to have superior merits.

Histamine Injections.

The effect of histamine on gastric secretion will be discussed later. It is sufficient to record here that all cases which showed achlorhydria throughout an oatmeal gruel meal were at a later date re-examined. After a similar preparation the tube was passed and the resting juice withdrawn. A subcutaneous injection of I mgm of histamine hydrochloride was then given and gastric juice samples aspirated at half hourly intervals for two hours. Titrations were performed as before.

Hollander and Penner (5) point out that four distinct periods can be traced in the history of gastric analysis. Firstly the period prior to I883 when therapeutics played a more important part than diagnosis; Secondly the period (I883-I9I4) in which gastric analysis was carried out by the single aspiration of stomach contents after the ingestion of various foodstuffs in an attempt to find out details of their digestion and also the emptying time of the stomach.

The third period (I9I4 to the present day) essayed a diagnostic procedure based on a composite picture of the digestive work of the stomach as indicated by:-

(a) Secretory activity. (b) Degree of digestion (c) Emptying time.

In this period a small bore tube, repeated aspirations and a simple meal were introduced.

Finally there is developing at the present time an attempt to evolve a technique, essentially the same as the fractional test meal, but in which there is a specific modification of the fractional procedure for each physiological component and a statistical approach to the problem.

It is hoped to show later in this thesis that although gastric analysis cannot yield a sharply defined diagnostic method it can yield data which are an aid to diagnosis.

Anatomical and Physiological Considerations.

In order to understand fully the significance of gastric analysis, it is necessary to know the structure and physiology of the stomach and to take note of the current theories of gastric secretion.

Broadly speaking the stomach is divided into a larger cardiac part and a smaller pyloric part, divided by the incisura angularis on the lesser curvayure. From the physiologist's point of view however, the stomach is divided into the fundus, the corpus, the pyloric antrum, and the pylorus leading into the duodenal bulb, which latter may be regarded as an annexe to the stomach.

The stomach is lined with mucous membrane which is supported by a stroma of connective tissue, and is separated from the outer gastric wall by the muscularis mucosa.

The mucous membrane forms folds, between which are the gastric pits, crypts or foveolae gastrica and Babkin (6) states that on an average 4.3 gastric tubules open into each crypt.

The tubules are lined with epithelium. Each tubule has a narrow entrance or isthmus which is composed of mucous cells of little secretory activity, a neck which contains the mucoid cells and the majority of the parietal, oxyntic cells (so called because they secrete HCl or its precursor) and a body containing the chief or peptic cells.

Mucous cells are found in all parts of the stomach which is lined with a thin layer of mucus. All specimens of gastric contents are normally contaminated with mucus although the amount is less if the patient is prevented from swallowing his saliva. Several different muco-proteins are produced by the mucoid cells.

The glands at the extreme cardiac end of the stomach are tubular in shape and mostly mucoid. The chief, or peptic glands occupy the whole of the gastric mucosa exclusive of the cardiac and pyloric areas. The pyloric glands produce mucus and some pepsin. The pyloric juice is alkaline and its main function may be to reduce to some extent the acidity of the stomach contents.

The pyloric mucusa contains less pepsin than the fundus and corpus. The pyloric glands become larger as they approach the pylorus and become continuous with the small racemose glands of Brunner which occur in the submucous coat of the duodenum.

The Formation of Hydrochloric Acid.

There are various theories about the mode of production of HCl by the parietal glands and the main ones are worth quoting as the subject is intimately bound up with the interpretation of gastric analysis.

Bensley and his co-workers (7) state that the parietal cells secrete a protein hydrochloride. In the foveolae of the gastric mucosa this becomes hydrolysed with the liberation of HCl. The secretion of the gastric glands is progressively diluted as it passes along the glandular lumen by the secretion of the cells nearer to the neck of the glandular tubule.

Zimmermann's theory is that the parietal cells secrete an organic oxyphilic substance "acidogen" which does not mix with the secretion of the peptic cells. When it reaches the gastric crypts it is dissolved by an acidase produced by the epithelium of the foveolae and chlor-ions are liberated and participate in the formation of HCl.

Hollanders theory is that HCl is formed in that part of the cytoplasm of the parietal cells which is adjacent to the canalicular wall or in the wall itself. Chloride is taken by the parietal cells from the blood via the tissue fluid. The neutral chlorides present in the cytoplasm of the parietal cells are hydrolysed and the residual alkali is

immediately neutralised by the intracellular buffers.

These are the three main theories of acid secretion but there are a number of others which are mostly modifications of one or other of the above. They will be further discussed when considering neutralisation.

The Secretory Granules and their relationship to Digestive Enzymes.

Secretory cells can be divided into:-

I. A homogeneous structureless material.

2. Structures embedded in it--eg the mitochondria, Golgi apparatus, and the secretory granules, the latter being merely the products of the cell.

The secretory granules are probably of a colloid nature but are too big to be colloid particles. They are soft, easily flattened objects, consisting of a spherical vacuole, within which, surrounded by membrane, is a granule,

Langley in I88I stated that the amount of pepsin contained by any portion of the stomach is in direct proportion to the number of secretory granules contained by the chief cells of that portion in the living state.

The majority of authorities now believe that the granules chemically are not the specific organic substances of a protein or gluco-protein nature, but are the precursors of these substances.

Northrop has demonstrated the protein nature of pepsin and subscribes to the theory that there is an inert protein precursor of pepsin--called pepsinogen which is stored in the gastric mucosa and turned into pepsin by the action of HCl. This activation is suggested by the fact that pepsinogen is not impaired by alkalies whereas pepsin is impaired. On the other hand Waldschmidt-Leitz (8) considers that the unequal stability to alkali might be due to pH effects rather than to an alteration in the enzyme. However this may be, the important fact emerges that the activity of pepsin depends upon the presence of free HCl in the gastric juice. This point wil be further discussed when analysing the series of cases which are described in this thesis.

Ludwig in I85I discovered that the pressure in the occluded of the submaxillary gland may, after chorda tympani stimulation become greater than the blood pressure in the carotid artery. Therefore secretion is a process sui generis. It is essentially:-
I. The transfer of the water and crystalloids of the plasma through the glandular epithelium to the alimentary canal, sometimes plus products of cell synthesis--either organic eg bile salts, or inorganic, eg HCl.

2. Liberation by the glandular cells of the organic colloidal compounds which they have elaborated and which are often combined in the same way with enzymes, and solution of these substances in the passing fluid

Gastric juice as examined by fractional gastric analysis with the tube in the corpus of the stomach, is the secretion of the glands of the fundus and corpus with the addition of the mucous secretion of the epithelium lining these parts plus a variable amount of swallowed saliva.

The part that duodenal regurgitation and the juice of the pyloric glands plays will be considered later.

The gastric glands are organs of compound structure composed of different sets of epithelial cells, whose activity is regulated by different nerves or by various hormonal or chemical.

Babkin (9) states that the secretory work of the gastric glands is not regulated as a whole, but the final product of this activity-- the gastric juice--is dependent, especially as regards its composition, on the participation of various mechanisms - nervous or humeral that stimulate different parts of the glands. The conclusion may be reached that the qualitative changes which occur physiologically in the secretion in response to various stimuli are due to unequal quantitative activity of the different groups of secretory cells constituting these glands.

Regulation of Gastric Secretory Activity.

The following are the chief causes of secretion of juice by an empty stomach, as described by Babkin (IO)

I. Conditioned reflexes.

2. Swallowing of saliva and regurgitation into the stomach of duodenal juices. Pancreatic and intestinal juices and bile have been shown to stimulate gastric secretion.

3. Food residue in the stomach.

4. Mechanical stimulation of the mucosa of the pyloric part of the stomach.

5. Food masses in the intestines.

6. Probably in abnormal conditions there is an independent phase of gastric secretion after complete evacuation of the stomach.

7. Gases in the stomach.

8. Operative procedure.

9. Diseases of the skin or absorption of the contents of an abscess produce a continuous secretion of gastric juice in dogs.

The question of conditioned reflexes as a stimulus is one that is bound up intimately with the stimulus which may be termed 'psychological' amongst which may be included possible stimuli from the thought of eating, the sound of food being prepared or the association of ideas played by, for instance, the dinner gong . The part that this psychological stimulus plays is uncertain. Also

in doubt is the effect of emotion on gastric secretion in spite of oft quoted classical observations on one or two people with a gastric fistula. Floyer and Jennings (II) carried out a fractional gastric analysis on 20 normal students awaiting examination results, for one hour before and one hour after the results were made known. They reported that no abnormality which could be ascribed to anxiety, depression or elation could be demonstrated. This investigation was made in I946 and, apart from the small number of cases, it is possible that a generation which has just come through a World war requires a stronger stimulus. Wolff and Mittelman (I2) however, point out that there are various kinds of anxiety, such as that due to, or associated with hostility, resentment or aggression which may be accompanied by hyper-function, and that associated with depression, which may be accompanied by hypo-function of the stomach. It seems likely that, provided the stimulus is strong enough, this is correct.

The Reflex mechanism of the gastric secretion is as follows:- nervous impulses from the mouth cavity to the gastric glands are transmitted reflexly through the vagus nerves. Weak stimulation of the vagus produces a secretion of mucus which is slightly acid; strong stimulation of the vagus produces a strong secretion of HCl with pepsin. It is likely that the vagus has a direct communication with the peptic cells. Mucus is secreted

Independently of the nervous system but is greatly increased by its activity.

The afferent paths of the gastric secretory reflexes are probably the same as those for the salivary glands, ie the taste fibres of the 9th (glosso-pharyngeal) nerve and the lingual division of the 5th nerve (chorda tympani component) supplying the tongue; the buccinator branch of the mandibular nerve ; the palatine nerves from the facial nerve; and the pharyngeal branch of the vagus.

The sympathetic and parasympathetic nerves from the gastric nervous plexuses also supply the stomach but their exact relation to the secretory glands in the stomach is controversial.

Splanchnic nerve stimulation has been found to produce a thick mucous secretion of an alkaline reaction probably chiefly from the pyloric part of the stomach.

Zeljony and Savich in 1914 (13) and Savich in 1922 (14) showed that mechanical stimulation of the pyloric region greatly increased the concentration of pepsin in the gastric juice. This observation is obviously of importance in considering gastric function.

The secretory impulses conveyed to the gastric glands ~~xxxxxxx~~ by stimulation of the pyloric mucosa may be brought about either by nerve reflexes,or by certain chemical substances, which after being absorbed by the pyloric mucous membrane

are carried to the other parts of the gastric mucosa and there greatly increase the effect of vagal stimulation of the gastric glands. The theory has been postulated that there is a hormone which follows this course and Gaddum (I5) states that the hormone "Gastrin" is liberated from the pyloric mucosa and carried in the blood stream to provoke gastric secretion. He adds,however, that this may really be histamine.

Gastric secretion is affected by a number of chemical substances and fluids on direct contact with the gastric mucosa. Choline and lecithen (the latter of which liberates choline) both provoke gastric secretion after a latent period and both are contained in a large number of foodstuffs. Histamine,or a histamine like substance, is formed in gastric juice, but it is uncertain whether it is liberated as part of the normal secretory process by acetyl-choline, or whether it is liberated from the circulating blood or the gastric mucosa itself. The subcutaneous injection of histamine is the strongest stimulus to gastric secretion known, and this is made use of when performing gastric analysis by the histamine method. Histamine will provoke secretion afetr section of the vagi and theis tends to support the theory that the histamine, or histamine like substances, found in the gastric juice play an important part in

provoking secretion. The action of histamine is not negatived by atropine, but that of choline is. The theory discussed by Barsoum and Gaddum (I6) that the action of the vagus on the gastric glands causes the liberation of histamine, or histamine like substances, which stimulate the parietal cells fits many of the facts of gastric secretion, but obviously not all. It is also one of the properties of histamine that it causes dilation of capillaries with resultant stasis of blood, and in poisonous doses there may be agglutination of erythrocytes and exudation of plasma with de-vitalized mucous membrane. As Babkin (I7) points out, it is therefore a possibility that excessive liberation of histamine in the stomach might be a cause, or contributory cause of ulcer.

Experimentally Cowgill and Gilman (I8) showed that Vitamin BI is necessary for the secretion of gastric juice and that achyllia gastrica exists in beri-beri and pellagra. Experimentally, however, it has not been possible to diminish gastric secretion in man by feeding a Vitamin BI deficient diet. It has been shown that, within limits, gastric secretion varies directly in relation to the CO_2 content of the blood.

Pavlov established that there are many substances which, when introduced into the duodenum, cause gastric secretion, and it has come to be recognized that there is an intestinal phase of gastric secretion,

the mechanism of which is not clear, but which is known to be inhibited by atropine.

From the above the conclusion can be reached that there are many mechanisms which are capable of causing gastric secretion and that it is uncertain which of them,or how many of them, play a part in the normal digestive.

The role of Mucus.

Mucus is probably a colloid. It protects the mucous membrane from thermal,mechanical,or chemical damage. It has a moderate buffering action. It neutralises acid but also combines with it, and it is possible that acid,released when food first enters the stomach,is released from mucus to be later re-combined with it and released in the duodenum where it stimulates the flow of pancreatic juice. Pepsin is also easily adsorbed to adsorbed to mucus.

Washed mucus is indigestible,but mucus mixed with HCl and pepsin is slowly digested,some of the end products being cystéine,tyrosine and histadine.

Acid Neutralisation and Duodenal Regurgitation.

Frouin in I899 found experimentally that the concentration of total chloride in the gastric juice is practically constant, whereas the concentration of HCl and neutral chlorides varies in opposite directions according to the experimental conditions. He also showed that when the diet is deficient in sodium chloride the volume of gastric secretion gradually diminishes and the acidity diminishes whilst the neutral chloride rose, the total chloride remaining unchanged.

MacClean and Griffiths in I928 showed that the peptic power of the gastric juice rises as the neutral chloride increases and the acid decreases but this is only true for certain phases of digestion According to the same observers, the chlorine ion concentration of the gastric secretion is constant, being approximately equal to that of blood. Some of the chlorine is secreted as HCl and the rest as sodium chloride, most of it being the latter in the resting juice. As Hurst and Stuart (I9) point out, it is as least as likely that the gastric juice represents a mixture formed of acid from the fundus and corpus and alkali from the pyloric glands. They point out that the alkaline secretion from the duodenal bulb is probably quite insufficient to neutralise the acid chyme and that it is only when the chyme passes through the rest of the duodenum and meets the alkaline bile and pancreatic juice

that it becomes completely neutralised. The inference here is that the role of Brunners glands in the duodenal bulb is to lower acidity in the stomach through duodenal regurgitation rather than to neutralise the chyme in the duodenum, but in direct contradiction of this are the conclusions of Florey and Harding (20) who found that the secretion of Brunners glands could be drained in considerable amounts, especially from tied loops of duodenum in the rabbit. They found the secretion to possess a high alkalinity due to the presence of bi-carbonates and they made the suggestion that a failure of these glands was a factor in the production of duodenal ulcer.

A number of authorities, amongst them Rehfuss(21) agree with the theory first propounded by Boldyreff that the initial high acidity of the gastric juice of 0.32% to 0.48% is lowered to the optimum 0.15% to 0.2% by an influx of intestinal juice into the stomach. Impairment of the neutralisation factors, or a very excessive secretion rate of gastric juice, or pyloric obstruction would tend to render the acidity of the gastric contents equal to that of pure gastric juice; in other words to produce clinical hyper acidity.

Whatever may be thought of the possibility that hyperacidity is a cause or contributory cause of peptic ulcer, there is little doubt that it is of benefit to the ulcer patient if his acidity is neutralised by the intake of alkalies, and the

efficient working of the neutralising mechanism is of importance to the health of the body, whatever the factor or factors involved.

Pavlov's theory, propounded many years ago, is still supported by many, including Hollander at anyrate as regards theories. It is that the gastric juice issuing from the glands has a constant acidity, and the variations in gastric acidity are due to partial neutralisation by the alkaline mucus.

Rosemann's theory is that the acidity is not constant, but may undergo variations independently of the neutralising effect of the surface epithelium mucus. The total chloride concentration of the juice is practically constant. Two processes take place in the mucous membrane during the formation of HCl.

I. The accumulation of neutral chloride in the gastric mucosa.

2. The formation of HCl.

Therefore, concludes Rosemann, the gastric glands have the double function of concentrating chloride to a higher level than that of the blood or lymph, and of combining the chloride ion and the hydrogen ion to form HCl. Under the influence of stimulation the neutral chloride is hydrolysed into chloride and a base. The chloride combines with the H ion to form HCl. The stronger the stimulus, the more Cl is coupled with the H ion and the less appears in the secretion as neutral

chloride and vice versa. The base is returned to the blood. The total chloride content of the gastric juice is determined by the osmotic pressure of the blood and remains constant.

According to Eusterman and Balfour (21) however, Hollander has demolished Rosemann's theory by showing that the purest juice obtained from a fundus pouch does not contain any fixed base such as would be necessary if some precursor of acid were being split into acid and basic fragments, and furthermore that the pure juice is nothing but HCl and water and is isotonic with blood.

The vast majority of observers believe now that duodenal regurgitation plays a part in the variations of gastric acid and differ only in their views as to the importance of the part it plays. Medes and Wright(22) consider that regurgitation of the duodenal juice into the fasting stomach is a normal phenomenon.

Baird Campbell andHern (23) have shown that when the stomach is empty,the pyloric sphincter is relaxed,and duodenal contents regurgitate freely into the stomach,especially when the subject is lying down.

Bolton and Salmond (24) have shown that during the later phases of digestion there is normally anti-peristalsis in the duodenum causing regurgitation into the stomach.

Rehfuss (25) states that there are only 3 factors which can reduce acidity.

I. The diluting and neutralising effect of saliva.

2. The alkaline secretion of the pyloric mucosa.

3. The effect of duodenal regurgitation.

Ryle, approaching the problem from a different angle, believes that the important factors which produce hyperacidity are:-

I. An excess of secretion.

2. Pyloric hypertonus preventing the duodenal reflex.

Rehfuss (26) and his co-workers were able to demonstrate that there is almost constantly a tryptic enzyme, presumably trypsin, in the fasting and the digesting stomach. It was found that the trypsin value was high in the presence of low acidity and low in the presence of high acidity, and it was deduced from this that duodenal regurgitation was taking place, and that the alkaline duodenal juice was regulating acidity. They further showed that trypsin was present even when bile was absent and suggested that this might either be due to a difference in elimination of the bile and pancreatic secretions, or to the specific reflux of the pancreatic secretion alone.

Bolton and Goodhart (27) elaborated on this and made complete chloride estimations every quarter of an hour and showed that when the acidity in the

stomach reaches a certain average height, regurgitation of the duodenal contents occurs, and brings down the acidity curve by neutralisation. They assumed from this that it is a function of the pylorus to regulate the acidity of the gastric contents. They further state that in gastric analysis, although the percentage of protein HCl can be more or less estimated from the total acidity, no account is taken of the inorganic chloride which represents the HCl neutralised by alkali. Bolton strongly advocates the estimation of free HCl plus protein HCl plus inorganic chlorides, which represents as nearly as possible the percentage of total HCl secreted, and is, according to Bolton the real secretory curve. He is of the opinion that as this organic chloride has been formed by neutralisation, its quantity bears on the relaxation of the pyloric sphincter.
Boyd (28) accepts duodenal regurgitation as being the prime, if not the only factor in acid neutralisation.
However as has been recorded, it is by no means universally accepted that this is the only factor in altering gastric acidity.

Cannon (29) demonstrated that the stomach is evacuated by occasional discharges of chyme through the pylorus and not every peristaltic wave gives rise to pyloric relaxation. He demonstrated that acid in the pyloric antrum, when it reaches a

certain concentration, opens the pylorus, and when the acid in the duodenum is neutralised the pylorus closes.

Although Cannon produced a number of convincing experiments to support his observations he does not seem fully to have established cause and effect. Moreover, observations by Carlson and Litt (30) on animals and by Baird Campbell and Hern (31) on men, do not support the theory of acid control of the pylorus.

MacLean and his co-workers(32) deny the importance of regurgitation as a factor in diminishing free acidity in the later specimens and state that in the isolated Pavlov pouch a similar falling off in acidity occurs together with a rise in the neutral chlorides, and they attribute this to an actual secretion of neutral chlorides by the stomach

Work by Shay, Katz and Schloss (33) tends to support this as also does the work of Maclagan (34).

The question of neutralisation still appears to lack a definite answer. It appears probable that more than one factor is involved. There is no room for doubt that duodenal regurgitation does take place at anyrate in a majority of people. It can be fairly convincingly demonstrated, at anyrate to most radiologists satisfaction, by X.Ray screening after a barium meal. The presence of bile and a tryptic enzyme in aspirated stomach contents before the stomach has emptied itself of a gruel test

meal is a commonly observed phenomenon. As will be seen in the table of this series of cases, bile appears in the stomach contents before the stomach has emptied in 20 out of 100 cases of duodenal ulcer, in 6 out of 17 cases of gastric ulcer and in 14 out of 81 cases of functional dyspepsia. It is difficult to see how this bile could be present except by regurgitation, in such a high proportion of cases. One is faced then with the fact that there is, at some stage of digestion, a flowing back of some of the duodenal contents into the stomach. It follows therefore that these duodenal contents, which have met and mixed with the alkaline secretion of Brunner's glands and in many cases the alkaline bile and pancreatic juice also, must bring back into the stomach some alkali and this, in turn, must be responsible to some extent in lowering gastric acidity. Whether this is the only mechanism or whether there are others, still remains a debated point.

Alvarez (35) accepts this regurgitation as playing a part in lowering acidity and states that he has often seen it taking place radiographically, and he stresses the significance of the experiment of Ivy who found that a segment of duodenum or jejunum 35cm long can, in an hour, neutralise half of the free acid in 150 cc of decinormal H Cl.

Interpretation of Gastric Analysis Charts.

Many authors, when writing on the subject of gastric analysis, fail to make it clear what they regard as normal standards. Cases are said to show hyperchlorhydria without it being made apparent what the writer takes as constituting such a diagnosis. A further anomaly occurs in the actual method of titration. There is a small difference in the readings of the burette if the titration, using Topfer's reagent is carried through until a universal persistent canary colour is obtained instead of a trace of this colour, as recommended by some writers, and again, when using phenolphthalein if the titration is carried through until a universal persistent pink colour is obtained instead of a trace. The difference is small (about 0.2cc of decinormal NaOH) but it is recorded here that the Author in all these cases carried through the titration until the respective colours were universal.

In the quantitative examination the Author has followed the classification of Bell as described by Harrison (36) which is as follows:-

Achlorhydria. Never any free HCl

Hypochlorhydria. Free HCl never above 10 N/10 per cent

Hyperchlorhydria. One or more points on the curve above 60 cc N/10 per cent.

In view of the number of border line cases and the fact that in some cases the free HCl just reaches the 60 figure at one point, without the general curve beimg that of hyperchlorhydria, whereas in other cases the general curve is high without ever quite reaching 60, the Author has made slight modifications in the cases described on Bell's classification. Cases where the free HCl curve is at 2 points at 60cc N/IO per cent or higher are called "hyperchlorhydria". Cases where the curve is at one point at 60 and at one point between 50 and 60 or at two or more points between 50 and 60 are called "mild hyperchlorhydria". In actual fact examination of these cases using Bell's classification strictly, makes practically no difference in the final results as classified by the Author's method. It is felt, however, that to label a case "hyperchlorhydria" when the only evidence of this is that the curve at one point touches the 60 mark and for the rest of the time is within normal limits, is to give a false impression and it is felt that the insertion of the word "mild" is justified.

The suggestion that pylorospasm is present when looking at a fractional test meal chart depends in the Author's opinion on there being present two factors. These are (a) delayed emptying of the stomach as shown by the presence of starch

up to and beyond 3 hours after giving the test meal and (b) associated with this, a persistently high acid curve, or a rising acid curve. It is not in the Authors opinion, necessary for hyperchlorhydria to be present to diagnose pylorospasm so long as the acid curve remains high or rising and there is delayed emptying.
Such a hypothesis favours the theory that the lowering of the free acid towards the end of gastric digestion depends to a large extent on duodenal regurgitation and is also compatible with the supposition that partial neutralisation occurs due to mucus. If either of these theories were incorrect it would mean that in the first place, with duodenal regurgitation playing no part in neutralisation, there would be no good reason for the acid values remaining high in pylorospasm; in the second case, with mucus playing no part, the acid values would soar as digestion progressed. The theory that the stomach itself secretes a base towards the end of digestion has fallen into disrepute at present as has been discussed earlier.
The estimation of neutral chlorides has not been performed in this series of cases. It is true that this estimation represents the true secretory curve of the stomach, but this information

is of little use to the clinician. There can be no suggestion that chlorides either cause or aggravate peptic ulcers. The information which the clinician requires is not the quantity of the secretion of the stomach, but the amount of the secretion which remains unneutralised as free acid, coupled with as much information as possible about the working of the stomach.

The present series of cases will now be examined, firstly as a whole, and secondly, under the separate diagnostic headings.

The average age of the cases under review is 25 years.

Taking the 284 cases as a whole, and remembering that the one thing they all have in common is symptoms of dyspepsia, the only comparison of interest is one with a series of gastric analysis investigations in normal people below middle age. Bennett and Ryles classical investigation of 100 healthy young males, may be conveniently taken for comparison. From these cases the limits of free HCl in 80% of healthy males is recorded as a shaded area on most fractional test meal charts. Bennett and Ryle employed a similar technique to that of the Author and it is of interest to record that in the re-examination of some of their cases, they found that the curve was remarkably constant in contrast to the findings of some other authorities who state that there are great variations in the type of curve in the same individual examined at various times under the same conditions. Beaumont and Dodds (37) point out that it is very doubtful if these alterations are of a type that would simulate pathological curves.

In the Author's series, 26 cases were re-examined

all within 14 days and in similar conditions. The general type of curve was remarkably similar to that first obtained, in 21 of these cases. 4 of the cases showed a considerably higher acid curve and a quicker emptying time, probably because of nervousness and difficulty in swallowing the tube at the first examination. The remaining case showed achlorhydria at the first examination and a normal curve of acidity at the second examination.

On the other hand, as would be expected, in 14 cases which were re-examined after being under treatment for an average of two weeks with alkalies, atropine and a suitable diet, the fractional gastric analysis picture was very different. All these cases were proved duodenal ulcers exhibiting pylorospasm. It was found that 7 of these cases (50%) showed a quickened emptying time by 30 minutes, with slightly lower acid curves; 2 showed a quickened emptying time by 30 minutes with greatly reduced acid curves; 2 showed a slightly lower curve and the same emptying time. The remaining 3 showed charts bearing no great resemblance to the original ones.

The following table shows an analysis of the fractional test meal findings in the whole series of cases divided up into their various diagnoses.

Diagnosis.	Duodenal ulcer.	Gastric ulcer	Anastamotic ulcer.	Gastritis.	Gastro-duodenitis	Duodenitis.	Functional dyspepsia.	Nervous dyspepsia.	Miscellaneous.
Av. Vol. Resting Juice.....	57cc	50cc	45cc	49cc	49cc	41cc	42cc	56cc	40cc.
Hyperchlorhydria	41	7	I	2	3	4	8	6	2.
Mild Hyperchlorhydria....	I9	0	-	3	5	I	8	5	2
Hypochlorhydria.	4	3	-	4	I	0	I7	2	I
Achlorhydria (after Hist)	-	-	I	-	-	-	3	I	2
Isochlorhydria	36	7	-	6	4	5	45	I6	9
Pylorospasm.	33	2	-	-	I	3	-	-	I
Pylorospasm associated with hyperchlorhydria.	I3	2	-	-	I	I	-	-	-
Excess mucus.	2	-	-	4	-	-	2	-	-
Moderate mucus	82	I3	2	II	I2	8	67	28	I3
Little or no mucus	I6	4	-	-	I	2	I2	2	3
Numbers with little mucus which were:-									
(a) hyperchlorhydria.	7	3	-	-	-	I	I	I	I
(b) mild "	3	-	-	-	-	-	-	-	I
(c) isochlorhydria	6	I	-	-	-	I	6	-	-
Average emptying time.	2-2½hrs	2hrs	3+hrs	2 hrs	2-2½hrs	2-2½hrs	I½-2hrs	2-2½hrs.	I½-2 hrs.
Delayed emptying over 3 hours.	34	3	2	-	2	I	20	I	4
Empty below 2 hours.	39	5	-	5	5	3	32	2	4
Bile appearing before stomach empties.	20	6	2	3	I	0	I4	0	I
Number of cases	I00	I7	2	I5	I3	I0	8I	30	I6

Table I.

It is realised that the number of cases in some of the groups shown in Table I is too small for any convincing conclusoins to be drawn from them. Accordingly they will be dealt with briefly and without any undue significance being attached to the results. The groups in question are:-

I, Anastamotic Ulcers.

There are only two cases here. In one of them the stoma was functioning well and, as might be expected, there is bile in the stomach contents throughout, and achlorhydria, due doubtless to neutralisation by the alkaline bile and pancreatic juice. The appearance of starch up to 3 hours was clearly due to regurgitation of the meal into the stomach through the stoma, rather than to any primary delay in emptying. In the other case the stoma was functioning very poorly or not at all and there was hyperchlorhydria with some delay in emptying.

2. Miscellaneous Cases.

These are I6 in number and are only included because they help to make up a composite picture of dyspepsia as a whole. Six of the cases were due to chronic appendicitis, three to post operative adhesions and two to gall stones. There was one carcinoma of the stomach.

The figures given in Table I are of all the cases investigated and, as has already been mentioned, include groups of cases which are too small in number for conclusions to be usefully drawn from them individually. The larger groups will be the subject of a later table, with a more detailed discussion.

Of the cases shown here it will be seen that hyperchlorhydria occurs in 41% of the 100 cases of duodenal ulcer and in 41% also of the cases of gastric ulcer. The percentage of hyperchlorhydria occurring in the small number of cases of gastro-duodenitis and duodenitis is however much the same, but the figure for the cases of functional and nervous dyspepsia falls to about 13%

Hypochlorhydria is however, rare in cases of duodenal ulcer, only 4% being recorded as opposed to 20.7% of the functional and nervous dyspepsia cases. Hypochlorhydria was found in duodenal ulcer cases when there was free duodenal regurgitation as shown by the presence of bile in some of the specimens. This was also true for a number of the cases of hypochlorhydria found in functional dyspepsia. Mucus was practically absent in 16% of the duodenal ulcer cases and of these 16 cases only 6 showed isochlorhydria, the rest showing more or less severe degrees of hyperchlorhydria, and this

tends, perhaps, to support the contention that the alkaline mucus plays an important part in diminishing gastric acidity.

Duodenal regurgitation, as shown by the appearance of bile in the specimens before the stomach empties was demonstrable in 20% of the duodenal ulcer cases and 30% of the gastric ulcer cases. It was observed in only one of the twenty three cases of gastro-duodenitis or duodenitis, and did not appear at all in the cases of nervous dyspepsia. In the cases of functional dyspepsia the percentage figure was the same approximately as for the duodenal ulcer cases. The appearance of bile obviously is to a large extent dependent on there being no pyloric obstruction or pylorospasm to hinder regurgitation.

The most striking figures in Table I relate to the incidence of pylorospasm. The Author in reading the charts and making his report gave an opinion as to the probable presence of pylorospasm based entirely on what was to be seen on the chart and before the X Ray findings were known. It is therefore of interest to note that pylorospasm was considered to be present in 33% of cases which were later confirmed as duodenal ulcers, in 2 out of 17 cases of gastric ulcer, both with the ulcer near to the pylorus, in one out of 13 cases of gastroduodenitis and in 3 out

of IO cases of duodenitis. It was not considered to be present in any of the cases of functional or nervous dyspepsia. It may be claimed therefore with some confidence that here is an aid to diagnosis of considerable value. Essentially it is an indication of organic disease somewhere in the digestive system, more specifically it concentrates the attention of the observer to looking for a lesion near to the pylorus or in the duodenum, more particularly the duodenal bulb.

It is felt that of all the information that can be obtained from gastric analysis, the manner of working of the pylorus is the most useful and the most significant finding that can be obtained apart from a study of the resting juice in patients with gastric cancer and the absolute achlorhydria of cases of pernicious anaemia.

Of the rest of the cases in Table I it is intended to say little. In the miscellaneous group there was one case of gastric carcinoma with the typical foul smelling resting juice, containing plentiful debris and lactic acid, and achlorhydria throughout (the latter not a constant finding in cases of this sort in the early stages. Such cases come within the scope of the surgeon and will not be further discussed.

Another case in the miscellaneous group was a man complaining of vague dyspeptic symptoms together with shortness of breath. The case showed an absolute achlorhydria even after histamine and on blood examination was found to be a case of pernicious anaemia, a fact which was suspected from the start although the age of the patient was against such a diagnosis. The other miscellaneous cases are too few in number to warrant description and of little interest anyway.

The main feature of the functional dyspepsia cases was the fact that practically all of them cleared up more or less rapidly on a suitable diet coupled with rest in bed and the administration of alkalies. It is of course likely that some of these cases later relapsed after return to a life unsuited to those prone to digestive disorders.

With regard to the above table, it is perhaps justifiable to include as one group the cases shown as 'functional dyspepsia' and 'nervous dyspepsia'. The two groups of cases have in common the fact that all the patients suffered from well marked symptoms of dyspepsia for which careful clinical examination accompanied by laboratory investigations and radiological examinations have failed to find an organic basis. Of course there may be, and probably is some process taking place in the body, of a temporary nature, which is pathological but not demonstrable by present day methods as a definite organic abnormality. The patient suffers from pain which undoubtedly is a real pain caused by some more or less temporary disorder in the function of the stomach or duodenum. Such cases are only termed 'functional' because we are at present unable to determine exactly which of the digestive processes is behaving abnormally. It may well be that at some future date, methods of investigation will be evolved which will enable us to give a more exact diagnosis of these cases and to exchange symptomatic treatment of these cases for treatment based on knowledge of what exactly is causing the dyspepsia of the patient. The difference between the 'functional' dyspepsias of this series and the cases labelled 'nervous'

dyspepsia,is that in the latter cases well marked anxiety symptoms have been present,of which the dyspeptic symptoms have only been a part. Cases so named in this series have had anxiety symptoms severe enough to impress the author in his capacity as a physician and have afterwards been examined and the diagnosis confirmed by a psychiatrist. The cases labelled 'functional'dyspepsia and the cases where organic disease has been found,have not, with a few exceptions,been examined by a psychiatrist. The reason for this was that,for the series of cases under review,diagnosis was of more importance than aetiology. Moreover the patients were all people exposed to the mental stress and strain of service in the Royal Navy in wartime. It is highly probable that expert psychiatrists would find some symptoms of anxiety in all the patients examined in this series. It is the Author's firm conviction based on personal experience,that at the end of a trying and lengthy period at sea in wartime,nobody can be considered to be absolutely normal from a psychiatrist's point of view.

Many workers have tried to demonstrate with more or less success,that there is a profound connection between worry and peptic ulcer,particularly duodenal ulcer. It is shown statistically that a period of worry often precedes a period of

activity in a duodenal ulcer that has been quiescent. Such considerations are beyond the scope of this thesis, but are worth bearing in mind when the justification of diagnosing a case as 'nervous' dyspepsia is called to question. As has been mentioned however it is justifiable in this series to combine the cases of 'functional' and 'nervous' dyspepsia into one group, making a total of III cases in the group. This number may be conveniently compared with the other large group of I00 cases of duodenal ulcer. Such figures are large enough for conclusions to be drawn from them, which does not apply to the other groups of cases in this series except in so far as they can be regarded as a whole as cases of dyspepsia. The two large groups referred to above may also be compared incidentally with the I00 cases of fractional gastric analysis on healthy young males performed by Bennett and Ryle at Guy's Hospital in I92I whose technique was essentially similar to that of the Author and whose findings have for so long been accepted asa a standard of normality for this type of test meal.

The table set out on the next page elaborates on this.

Diagnosis.	Duodenal Ulcer	Functional and Nervous Dyspepsia	Normal (Bennett & Ryle)
Average Vol. of Resting juice.	57cc	40cc	Average not given as 54 cc varied from 20cc to 100 cc.
Hyperchlorhydria	41 %	13.5 %	10 %.
Mild hyperchlorhydria.	19 %	11.6 %	
Isochlorhydria	36 %	55.0 %	80 %
Hypochlorhydria.	4 %	20.7 %	10 %
Pylorospasm.	33 %	0	0
Average emptying time.	2-2½ hrs	2 hrs	2 hrs.
Number of cases.	100	111	100

Table 2.

Table 2 shows several significant figures. 60 % of cases of duodenal ulcer in this series show hyperchlorhydria although I9 %were only mild hyperchlorhydria. This is to be compared with 25.I% of hyperchlorhydrias in the functional and nervous group,of which II.6% were only mild hyperchlorhydria,and I0% in Bennett and Ryle's series of normal cases. Harrison (36) has published figures compiled from the results obtained by a number of workers.His figures for I35 cases of duodenal ulcer show that Hyperchlorhydria was present in 50.3%, isochlorhydria in 43.7% and hypochlorhydria in 3%. Most workers however give much higher figures for hyperchlorhydria in cases of duodenal ulcer. Rehfuss considers that 80% of cases have hyperchlorhydria but it is not clear whether he accepted Bell's classification. It is suggested that in the author's series of cases the duration of symptoms was probably much shorter before these cases were investigated than is the case in patients met with in civilian hospitals. It is no uncommon thing for a patient to be given alkalies at intervals for years by the family doctor before the occurrence of an unusually acute phase in the complaint draws the attention of the latter to the desirability of hospital investigation. The frequent remissions of symptoms and the periodicity which is such a frequent feature in duodenal ulcer also leads

both doctor and patient astray. There is however no place for the man in wartime in the Services who is not completely fit or who is constantly having to attend at Sick Quarters and so cases of persisent cases of dyspepsia are investigated much earlier. There is also no room for doubt that something connected with Service conditions in the recent War caused a great increase in the numbers of cases of dyspepsia especially cases of duodenal ulcer. The cases investigated were therefore, for the most part, those with a comparatively short history and therefore one did not find so many cases of old standing chronic duodenal ulcer with pyloric obstruction which is the type of case most likely to give high acid values. Pylorospasm, nevertheless, was judged to be present in 33% of duodenal ulcer cases, and not to be present in any of the cases of functional dyspepsia. It is considered that pylorospasm is always a sign of organic disease somewhere in the digestive system, usually resulting directly from an ulcer near to the pylorus but sometimes occurring reflexly from a more distant lesion. It was thought to be present in 3 cases which were considered to be duodenitis and in one case of dyspepsia associated with chronic appendicitis. However, as has already been remarked upon when discussing the figures shown in Table I , pylorospasm is overwhelmingly confined to cases of duodenal

ulcer,ulcers near the pylorus,and the rather more obscure complaint of duodenitis.

The average emptying time of cases of functional dyspepsia does not differ from that of normal cases,but the average emptying time of duodenal ulcer cases is about half an hour longer,the figure being,of course raised by the large number of cases with pylorospasm.

As regards the volume of the Resting juice, the figures are not particularly significant when taken as an average. The average is certainly I7 cc higher than for cases of functional dyspepsia but the figure is raised to its high average of 57cc by a comparatively few cases in which the volume of juice was unusually high,such cases being probably those with some degree of pyloric obstruction.

In conclusion it may be said that the cases of duodenal ulcer as compared with the cases of functional dyspepsia,showed a higher proportion with hyperchlorhydria,though not such a high proportion as has been obtained by some other observers,a slightly longer average emptying time,a slightly higher volume of Resting juice, and the presence of pylorospasm in a third of the ulcer cases as compared with its complete absence in cases of functional dyspepsia.

It is,perhaps,tempting on examining charts of gastric analysis patients,particularly those of patients with duodenal ulcers,to try to explain some of the symptoms of which the patient complains by reference to the working of the stomach as shown by a fractional analysis chart. A few minutes reflection will,however,enable the observer to realise the limitations in the data from which he can draw his conclusions. Any form of test meal is,in fact,an artificial stimulation of the stomach's secretory powers, no matter what laboratory examinations are made of the specimens obtained. The composition of the test meals bears no relation either chemically or in form to the ordinary mixed diet meal consumed even by the peptic ulcer sufferer who is restricting his diet. The most unnatural of all test meals is probably the alcohol meal. Nobody,least of all the ulcer patient,lives on a diet of 7% alcohol. The test using a subcutaneous injection of histamine is also at first sight an unnatural one,but it must be remembered that,as has already been described,it is thought by many that liberation of histamine is part of the normal mechanism of stimulation of the gastric glands. It is not claimed that oatmeal gruel resembles in its composition a normal mixed diet but it is not so wildly dissimilar as the stimuli named above.

One can say with certainty however that any significance attached to the acid curves of a test meal chart in the way of attempting to correlate the acid variations with the onset of pain as described by the patient, must be of little value owing to the difference in composition between any test meal and a mixed diet.

The duodenal ulcer cases in this series were examined to see if there were any relationship, bearing the observations above in mind and with the following results;-

Number of Cases.	I00.
Cases in which the time of onset of pain coincided with a sharp rise in the free acid.	30
Cases in which the time of onset of pain coincided with a sharp fall in the free acid such as might be brought about by the commencing emptying of the stomach.	36
Cases in which there is no apparent relationship.	34
Cases in which the pain comes on after the stomach has emptied.	I7
Cases in which the pain is late in onset, prolonged, and associated with pylorospasm.	7

It is not felt that the above figures have any significance and it is concluded that it is not possible to correlate symptoms complained of by the patient after meals of a mixed diet with findings after a gruel meal.

The Type of fractional test meal chart seen in the various digestive disorders.

The important question must now be answered, as far as possible, as to whether there is, or is not a typical fractional analysis chart for all or any of the various diseases associated with the digestive system.

Let it be said straight away, that in cases of carcinoma of the stomach, particularly in the later stages, there is a typical chart. The findings are too well known to require further elucidation here, especially as only one such case appears in this series. The finding of foul smelling debris and blood in the resting juice, lactic acid, and the usual but not invariable absolute achlorhydria resulting from destruction of the stomach tissues, are facts beyond dispute. Gastric analysis is invaluable in cases of this sort as an aid to diagnosis and is decisive in cases with doubtful radiological findings.

Of almost equal value is the finding of absolute achlorhydria in cases of suspected pernicious anaemia. It may be mentioned, however, that a macrocytic anaemia with many of the features of pernicious anaemia, but with normal gastric acidity has been described.

The gastric analysis findings during the course of some of the fevers, deficiency diseases and some tropical diseases are interesting but are

beyond the scope of this thesis.

There remains the findings in the types of dyspepsia described in this thesis.

There has become a kind of tradition in many of the standard text books on Medicine that there is a typical acid curve in response to a gruel meal for most of the commoner conditions met with in the stomach and duodenum. One can pick up half a dozen text books and see the same charts reproduced in each and each chart being described as typical of a certain condition. The Author has come to the conclusion that this is to a large extent erroneous and creates a false impression in the mind of the student which is hard to eradicate.

The chart shown as typical of duodenal ulcer is one in which the free acid curve, not high in the resting juice, falls sharply after the meal is administered, then rises sharply to hyperchlorhydria for an hour or more, falls sharply as the stomach begins to empty and finally rises to hyperchlorhydria again as, and after the stomach empties. The stomach is given as emptying about 2¼ hours after the test commences. Bile is absent throughout, and there is little or no mucus.

Now, analysing this chart, one can form certain conclusions from it. There is a hyperchlorhydric

response to the meal, there is no particular evidence of pylorospasm,-stomach emptying is not delayed unduly and the acid level falls as the stomach starts to empty, presumably owing to partial neutralisation which most authorities agree is due to duodenal regurgitation. At the same time, regurgitation is not a marked feature as bile is absent. The fall might be due to an actual lessening of secretion but the total acid curve is shown as not falling to the same extent. Finally there is the rise in acidity as, and after the stomach empties which probably signifies the "intestinal" phase of secretion which has been discussed previously in this thesis.

A second type of chart is shown by some authors as being typical of duodenal ulcer. This is one in which the acid curve climbs rapidly to a hyperchlorhydric level, maintains this level in a high plateau type of curve with a little falling off towards the end. There is delay in stomach emptying, bile is absent and mucus slight or absent. It is clear that this is a chart of pylorospasm, or pyloric obstruction. The commonest cause is probably duodenal ulcer, but this is only because duodenal ulcer is the most commonly met with. A pyloric ulcer, or any cause of pylorospasm might equally well give the same finding.

Taking the ICC duodenal ulcer charts in this

series,it is found that only I5 xrx closely resemble one or other of these types although the 33 judged to have pylorospasm may be said to show a persistently high acid curve with delayed emptying and therefore to resemble somewhat the plateau type of curve.

As regards the other findings,an appreciable amount of mucus was found in 82% of the duodenal ulcer cases,and bile appeared before the stomach emptied in 20%. Moreover a number of the most active ulcer cases as judged by the severity of the symptoms and such factors as recent haematemesis,occult blood in the stools, and marked epigastric tenderness,showed curves in no way typical of the conventionally accepted duodenal ulcer charts.

The gastric ulcer cases are too few in number (only I7) for the Author to draw conclusions.

Cases of duodenitis,an entity which some of the authorities deny exists,show no feature in their charts which is not seen in duodenal ulcer charts. The diagnosis was made by their having the symptoms suggestive of a duodenal ulcer,but no crater being demonstrable by X.Ray and a marked general tenderness of the duodenum being present when palpated under the X.Ray screen xfxtr after a barium meal.

Another type of case worth mentioning,is that diagnosed as Gastritis. The history and symptoms here are shared in importance by the personal habits of the patient. The type of chart found here usually resembled the text book chart,ie excess of mucus,a low or fairly low free acid curve,no pylorospasm,frequent evidence of regurgitation and a quickened emptying rate, although this latter characteristic was not universally present in the small number of cases coming under this heading in the present series.

Cases with gastroptosis,usually part of a general visceroptosis,showed delayed emptying but with no persistently high acid curve. The cases were usually women in the W.R.N.S.

Summary.

I. A study has been made of the Fractional Test Meal findings of 284 cases of dyspepsia in the Royal Navy, including 100 cases of Duodenal Ulcer.

2. A full description of the methods used and the standard of diagnosis required has been given.

3. A study has been made of the various theories of gastric neutralisation and secretion. It is considered that no theory yet advanced fully explains all the factors involved.

4. The relationship between symptoms and test meal findings has been investigated. It is found that there can be no significant relationship between the symptoms of a patient on a mixed diet and the response shown to a gruel meal.

5. A comparison between the findings in duodenal ulcer cases and those in other forms of dyspepsia has been made, and the findings compared with the results obtained by other workers. It is concluded that a typical duodenal ulcer fractional test meal chart does not exist. The classical duodenal ulcer charts of textbooks owe their form to the presence of factors not necessarily exclusive to duodenal ulcers, one of which is pylorospasm.

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